REMARKS.

Reconsideration of the above-identified application in view of the foregoing amendments and the following remarks is respectfully requested.

A. Status of Claims

Claims 1-3, 5, 7, 8, 11, 12, 15, 30, 31, 33, 35, 36, 39, 40, 42 and 44-47 are pending. By this paper, claims 12, 39, 40, 42, and 44-47 are amended.

Claim 12 is amended to recite: "[a] quality assurance method according to claim 11, wherein the probe chip, for which quality is assured, is a probe carrier produced by . . ." Claims 39, 40, 42, and 44-47 are similarly amended. Claim 46 is also amended to add the phase, "produced by a producing system". Support for these amendments is found throughout the application as originally filed, including, for example, on page 55.

Claims 40, 42, 44 and 45 are also amended to add the word, "and". Claim 42 is amended to correct spelling (changing "chips" to "chip). Claim 44 is amended change an "a" to a "the". These amendments is not made for any substantial reason related to patentability (i.e., §§ 102, 103), and they are not intended to narrow claim scope.

No new matter is added with these amendments, and their entry is respectfully requested.

B. Rejections under 35 U.S.C. § 112 and 35 U.S.C. § 101

Claims 12, 39, 40, 42 and 44-47 were rejected under 35 U.S.C. §§ 112 as allegedly indefinite because it is allegedly "not clear whether a process of quality assurance or a product or a method of making the product" is claimed. (Office Action, p. 3-4). Claims 12, 39, 40, 42 and 44-47 were also rejected under 35 U.S.C. § 101 as allegedly indefinite because they are allegedly drawn to processes and products simultaneously. (Office Action, p. 4-5).

Applicants' respectfully traverse these rejections. In the interest of expediting prosecution, however, claims 12, 39, 40, 42 and 44-47 are amended by this paper to clarify that each of these claims is directed to a quality assurance method.

Specifically, amended claim 12 recites:

> "12. A quality assurance method according to claim 11, wherein the probe chip, for which quality is assured, is a probe carrier produced by
>
> (1) a step of preparing a purified probe;
>
> (2) a step of obtaining probe information on the purified probe;
>
> (3) a step of judging "good" or "not good" quality of each purified probe according to the obtained probe information and a predetermined criterion;
>
> (4) a step of obtaining a probe of which quality is "good" in case of the purified probe of which quality is judged as "not good";
>
> (5) a step of individually dissolving each purified probe judged as "good" in a solvent for ejection to a carrier, based on at least a part of the probe information obtained in (2), at a predetermined concentration and storing each obtained probe solution in an individual storing container;
>
> (6) a step of transferring each probe solution stored in said storing container to another container equipped in an apparatus for deposition onto the carrier;
>
> (7) a step of applying a surface treatment to the carrier for fixing the probe;
>
> (8) a step of depositing said probe solution onto a treated surface of said carrier by a method including following steps, thereby forming a plurality of mutually independent probe fixation areas;
>
> (8-1) a step of executing an analytical inspection on the carrier subjected to said surface treatment and judging "good" or "not good" state of said carrier according to the result of said analytical inspection and a predetermined criterion;
>
> (8-2) a step of depositing at least one selected from said plural probe solutions onto the carrier judged as "good"

so as to form a probe deposition area independent for each probe solution;

(8-3) a step of executing an inspection, concerning a formed state of the probe deposition area, on the carrier on which said probe deposition area is formed, and judging "good" or "not good" state of said deposition according the result of said inspection and a predetermined criterion;

(8-4) a step of executing, on the carrier having the probe deposition area judged as "good", a fixation of the probe to the surface of the carrier thereby obtaining a probe carrier;

(8-5) a step of executing an analytical inspection on the probe in at least one of the plural probe fixation areas constituted of probes fixed on said carrier; and

(8-6) a step of judging "good" or "not good" state of the produced probe carrier according to the result of said analytical inspection and a predetermined criterion."

Accordingly, Applicants' respectfully request withdrawal of the rejections, and respectfully submit that claims 12, 39, 40, 42 and 44-47 are in condition for allowance.

C. Rejection under 35 U.S.C. § 103(a)

Claims 1-3, 5, 7, 8, 11, 12, 15, 30, 31, 33, 35, 36, 39, 40, 42 and 44-47 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Tadashi Okamoto, Tomoshiro Suzuki, and Nobuko Yamamoto, "Microarray fabrication with covalent attachment of DNA using Bubble Jet technology", *Nature Biotechnology*, Vol. 18 (April 2000), at 438-441), (hereinafter, "Okamoto"), in view of WIPO Application Publication No. WO 99/39817 to Rava et al. ("Rava"). (Office Action, pp. 5-9). The rejection of claims 1-3, 5, 7, 8, 11, 12, 15, 30, 31, 33, 35, 36, 39, 40, 42 and 44-47 is respectfully traversed.

Specifically, Applicants' claim 2 recites:

"2. A method for producing a probe carrier comprising:

(a) a step of designing plural kinds of probes for detecting a target substance;

(b) a step of synthesizing the designed plural probes;

(c) a step of individually purifying the synthesized plural probes;

(d) a step of obtaining probe information on each purified probe;

(e) a step of judging "good" or "not good" state of synthesis and purification in each purified probe according to the obtained probe information and a predetermined criterion;

(f) a step of repeating the foregoing steps (b) to (e) on the purified probe of which state of synthesis and purification is judged as "not good", thereby obtaining "good" state of synthesis and purification in all the purified probes;

(g) a step of individually dissolving each purified probe judged as "good" in a solvent for ejection to a carrier, based on at least a part of the probe information obtained in (d), in a predetermined concentration and storing each obtained probe solution in an individual storing container;

(h) a step of transferring each probe solution stored in the storing container to another container equipped in an apparatus for deposition onto the carrier;

(i) a step of applying a surface treatment for fixing the probe to the carrier;

(j) a step of depositing the probe solution onto a treated surface of the carrier by a method including following steps, thereby forming a plurality of mutually independent probe fixation areas;

(j-1) a step of executing an analytical inspection on the carrier for judging "good" or "not good" state of the carrier according to the result of the analytical inspection and a predetermined criterion;

(j-2) a step of depositing at least one selected from plural probe solutions onto the carrier judged as "good" so as to form a probe deposition area independent for each probe solution;

(j-3) a step of executing an inspection, concerning a formed state of the probe deposition area, on the carrier on which the probe deposition area is formed, and judging "good" or "not good" state of the deposition according the result of the inspection and a predetermined criterion;

> (j-4) a step of executing, on the carrier having the probe deposition area judged as "good", a fixation of the probe to the surface of the carrier thereby obtaining a probe carrier;
>
> (j-5) a step of executing an analytical inspection on the probe in at least one of the plural probe fixation areas constituted of probes fixed on the carrier; and
>
> (j-6) a step of judging "good" or "not good" state of the produced probe carrier according to the result of the analytical inspection and a predetermined criterion."

Okamoto is directed to mircoarray fabrication with covalent attachment of DNA using Bubble Jet technology. Okamoto discloses that the following steps that were performed by the authors:

a. prepared and treated a glass substrate;

b. dissolved certain oligonucleotides in a certain solution, at a certain concentration;

c. placed the solution into tubes connected to an ink jet printer;

d. ejected the oligonucleotide solution onto the glass substrate as dots with a certain resolution.

(Okamoto, p. 438, para. 8 – 439, para. 1-2).

Okamoto also describes an investigation regarding the effects of ink jet ejection on DNA lengths and concentrations. (Okamoto, p. 438, para. 7). This investigation comprised using ink jet ejection to eject DNA fragments of varying lengths and sequences dissolved in a certain solution onto aluminum plates, and then examining recovered DNA to determine the range of bases and base pairs that could safely be ejected. (Okamoto, p. 438, para. 7). Ejected DNA solutions were also analyzed by HPLC for the purpose of confirming the absence of short oligonucleotides produced by shearing. (Okamoto, p. 438, para. 7). Okamoto, thus, describes a

one-time use of HPLC for investigatory purposes. Okamoto does not, however, disclose use of HPLC as a step in method of mircroarray fabrication.

To be more specific, the following steps were described by Okamoto in the one-time investigation described above:

i. 12 mer oligonucleotides were dissolved in a certain solution, at a certain concentration

ii. the solutions were placed in ink cartridges

iii. the cartridges were mounted on a printer

iv. an aluminum plate was mounted on the printer

v. the solution was spotted onto the plate onto a 3 x 5 inch area on the plate, with spotting conditions set to spot at a certain density and droplet volume

vi. the spotted oligonucleotide solutions were recovered from the aluminum plates with an aqueous buffer solution

vii. the spotted oligonucleotide solutions were purified by gel filtration

viii. the absorbances of recovered and purified oliogonucleotide solutions were compared with theoretical absorbances, or in an alternative step, recovered nucleic acid solutions were analyzed by HPLC.

(Okamoto, p. 438, para. 7; 440, para. 2; 441, para. 1-2).

The Office Action asserts that Okamoto teaches: "(c) a step of individually purifying the synthesized plural probes." (Office Action, p. 6). Applicants respectfully disagree. As evident from above, Okamoto does not teach a step of individually purifying the synthesized probes. Steps (i) through (vi), set forth above, clearly do not teach a step of "individually purifying the synthesized plural probes." Steps (vii) and (viii) do disclose steps directed to purification, but neither step (vii) nor step (viii), as described in Okamoto, teach individual purification of the probes, as recited in Applicants' claim 2. Indeed, steps (vii) and (viii) are

expressly directed to purification of "oligonucleotide solutions". They cannot therefore be directed to purification of individual probes.

Even assuming Okamoto does disclose "(c) a step of individually purifying the synthesized plural probes," which it does not, Okamoto does not teach this step be performed *before* dissolving probes in a solution and depositing onto a carrier, as recited in Applicants' claim 2. Specifically, Applicants' claim 2 recites "(d) a step of individually purifying the synthesized plural probes;" *before* "(g) a step of individually dissolving each purified probe . . . in a solvent for ejection to a carrier," and "(j) a step of depositing the probe solution onto a treated surface of the carrier." Indeed, both step (vii) and step (viii), as described above, and as described in Okamoto, are directed to purification of oligonucleotide solutions recovered after spotting onto aluminum plates. For this reason, Okamoto does not disclose, teach nor suggest the method recited in Applicants' claim 2, which recites "individually purifying the synthesized plural probes" and performing this step before "dissolving each purified probe . . . in a solvent for ejection to a carrier" and "depositing the probe solution onto a treated surface of the carrier."

The Office Action also asserts that Okamoto teaches: "(d) a step of obtaining probe information on each purified probe" and "(e) a step of judging 'good' or 'not good' state of synthesis and purification in each purified probe according to the obtained probe information and a predetermined criterion." (Office Action, p. 6). Applicants' respectfully disagree. Okamoto does not disclose these steps. For the reasons set forth above, Okamoto does not disclose "(c) a step of individually purifying the synthesized plural probes." Accordingly, Okamoto cannot teach a "(d) a step of obtaining probe information on each purified probe" and "(e) a step of judging 'good' or 'not good' state of synthesis and purification in each purified probe according to the obtained probe information and a predetermined criterion."

Even assuming Okamoto does disclose these steps, which it does not, it fails to teach performing "a step of obtaining probe information on each purified probe" and "a step of judging 'good' or 'not good' state of synthesis and purification . . . and a predetermined criterion" *before* "(g) a step of individually dissolving each purified probe judged as 'good' in a solvent for ejection . . . ," as recited in Applicant's claim 2. Indeed, Okamoto does not disclose any steps directed to obtaining probe information or judging synthesis or purification as 'good' or 'not good' until after the probes have been dissolved into solution, spotted onto aluminum plates and subsequently recovered. (Okamoto, p. 438, para. 7; 440, para. 2; 441, para. 1-2). Rather, the first step taught by Okamoto directed to purification of the probes—which is not directed to individual purification of the probes—occurs only *after* the oligonucleotides have been dissolved and subsequently spotted onto the aluminum plates and recovered from said plates.

The Office Action also asserts that Okamoto teaches: "(f) a step of repeating the foregoing steps (b) to (e) on the purified probe of which state of synthesis and purification is judged as 'not good', thereby obtaining 'good' state of synthesis and purification in all the purified probes Okamoto et al. teach repeating the steps with different probes," and "(g) a step of individually dissolving each purified probe judged as 'good' in a solvent for ejection to a carrier, based at least in part on the probe information obtained in (d)." (Office Action, p. 6). Okamoto does not teach a step of assessing probes as 'good' or 'not good', nor does it teach such a step occurring *before* dissolving probes in solution and depositing onto a carrier. Therefore, it also does not teach a step of repeating such assessments. Nor does it teach a step of dissolving only those probes judged to be 'good' in a solution.

For similar reasons, Okamoto also does not disclose elements of Applicants' step (j-2), recited in claim 2, as asserted in the Office Action, which includes "depositing at least one selected from plural probe solutions onto the carrier judged as 'good'," because Okamoto does not disclose a step of judging probes before deposition onto a carrier.

For similar reasons, Applicants' respectfully submit that Okamoto does not teach every elements of steps (j-4), (j-5), and (j-6), as those steps are described in the Office Action, p. 6, to the extent Okamoto does not teach a step of judging the probe carrier as "good" or "not good" distinctly from preparing and treating the carrier. Indeed, as admitted in the Office Action, "[r]egarding step (j-1), Okamoto et al. do not teach inspecting the carrier after the surface treatment." (Office Action, p. 8).

Accordingly, Okamoto does not disclose, teach or suggest every element of Applicants' claim 2, and therefore, Applicants' respectfully submit that claim 2 is in condition for allowance. For at least similar reasons, claims 1, 3, 5, 7, 8, 11, 12, 30, 31, 33, 36, 39, 40, 42 and 44-47 are also believed to be in condition for allowance.

Applicants have chosen in the interest of expediting prosecution of this patent application to distinguish the cited documents from the pending claims as set forth above. These statements should not be regarded in any way as admissions that the cited documents are, in fact, prior art. Likewise, Applicants have chosen not to swear behind the cited references or to otherwise submit evidence to traverse the rejection at this time. Applicants, however, reserve the right, as provided by 37 C.F.R. §§ 1.131 and 1.132, to do so in the future as appropriate. Finally, Applicants have not specifically addressed the rejections of the dependent claims. Applicants respectfully submit that the independent claims, from which they depend, are in condition for allowance as set forth above. Accordingly, the dependent claims also are in condition for

allowance. Applicants, however, reserve the right to address such rejections of the dependent claims in the future as appropriate.

CONCLUSION

Applicants respectfully request reconsideration and withdrawal of the rejection of Claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this response to Deposit Account No. 13-4500, Order No. 1232-5570. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,
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